INSIGHT: A PHASE 3, RANDOMIZED, OPEN-LABEL STUDY OF RIPRETINIB VS SUNITINIB IN PATIENTS WITH ADVANCED GASTROINTESTINAL STROMAL TUMOR PREVIOUSLY TREATED WITH IMATINIB WITH *KIT* EXON 11 + 17/18 MUTATIONS

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DISCLOSURES

- Prof. Bauer reports Honoraria from Novartis, Pfizer, Bayer, Pharmamar, GlaxoSmithKline, and Deciphera; consulting/advisory roles with Blueprint Medicines, Bayer, Lilly, Deciphera, Nanobiotix, Daiichi Sankyo, Exelixis, Janssen-Cilag, ADC Therapeutics, Mundipharma, GlaxoSmithKline, Adcendo, and Boehringer Ingelheim; research funding from Blueprint Medicines, Novartis, and Incyte (Institution); and funding for travel/accommodations/expenses from PharmaMar

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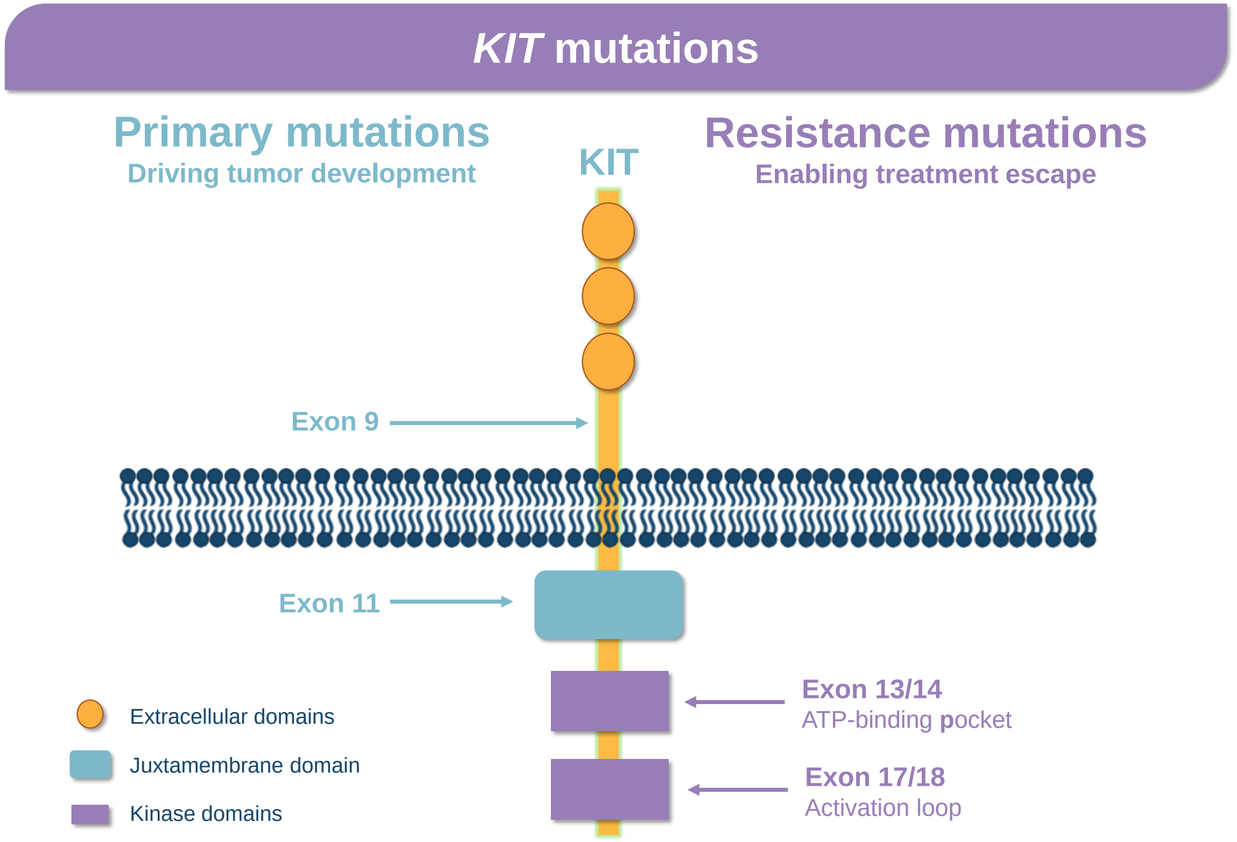
BACKGROUND

- GIST is the most common gastrointestinal sarcoma with ~80% of cases driven by *KIT* mutations[1]
- Imatinib, a TKI, is approved as first-line therapy for advanced GIST and leads to an objective response in ~50% of patients[2]
  - Many patients treated with imatinib eventually experience tumor progression due to the development of secondary mutations in the KIT ATP-binding pocket (encoded by exons 13/14) or activation loop (encoded by exons 17/18)[3,4]



1) Szucs Z, et al. *Future Oncol*. 2017;13:93-107. 2) GLEEVEC. Prescribing information. Novartis Pharmaceuticals Corporation; 2022. 3) Antonescu CR, et al. *Clin Cancer Res*. 2005;11:4182-90. 4) Kelly CM, et al. *J Hematol Oncol*. 2021;14:2.
ATP, adenosine triphosphate; GIST, gastrointestinal stromal tumor; TKI, tyrosine kinase inhibitor.

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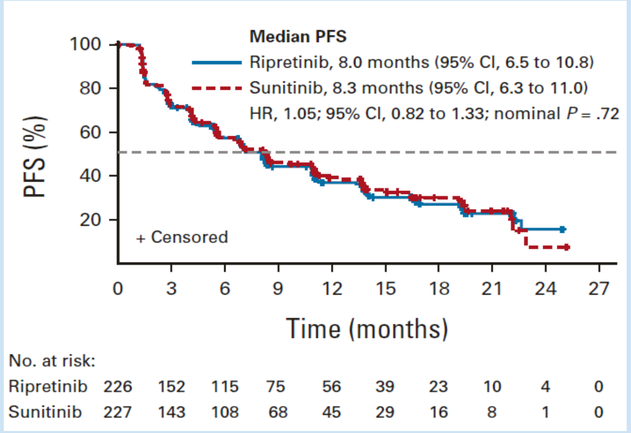
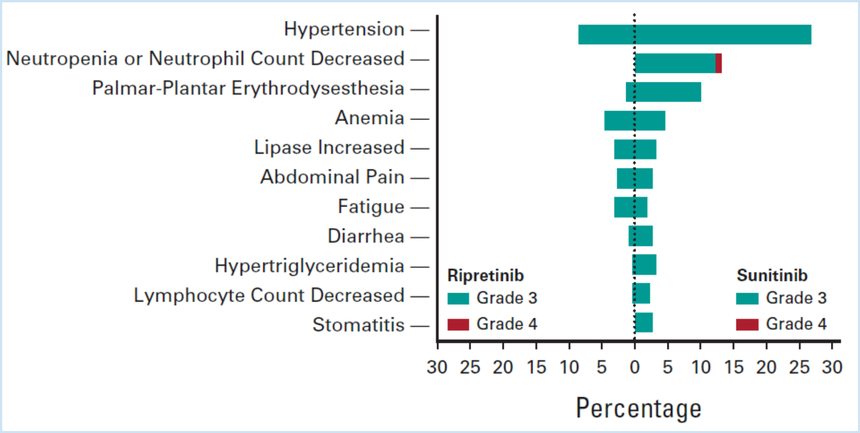
BACKGROUND

- Sunitinib is a multitargeted TKI approved as second-line therapy for advanced GIST after imatinib failure[1]
- Ripretinib is a broad-spectrum switch-control KIT/PDGFRA TKI approved for patients with advanced GIST who received prior treatment with 3 or more kinase inhibitors, including imatinib[2,3]
- In the phase 3 INTRIGUE trial (NCT03673501), the primary endpoint of superior PFS with ripretinib vs sunitinib was not met; however, ripretinib demonstrated comparable efficacy and a more favorable safety profile and better PROs compared with sunitinib in patients with advanced GIST previously treated with imatinib[4,5]



Bauer S, et al. *J Clin Oncol*. 2022;40:3918-28.



Bauer S, et al. *J Clin Oncol*. 2022;40:3918-28.

1) SUTENT. Prescribing information. Pfizer Laboratories; 2021. 2) Smith BD, et al. *Cancer Cell*. 2019;35:738-51. 3) QINLOCK. Prescribing information. Deciphera Pharmaceuticals, LLC; 2022. 4) Bauer S, et al. *J Clin Oncol*. 2022;40:3918-28. 5) Gelderblom H, et al. *Eur J Cancer*. 2023;192:113245.

GIST, gastrointestinal stromal tumor; PDGFRA, platelet-derived growth factor receptor alpha; PFS, progression-free survival; PRO, patient-reported outcome; TKI, tyrosine kinase inhibitor.

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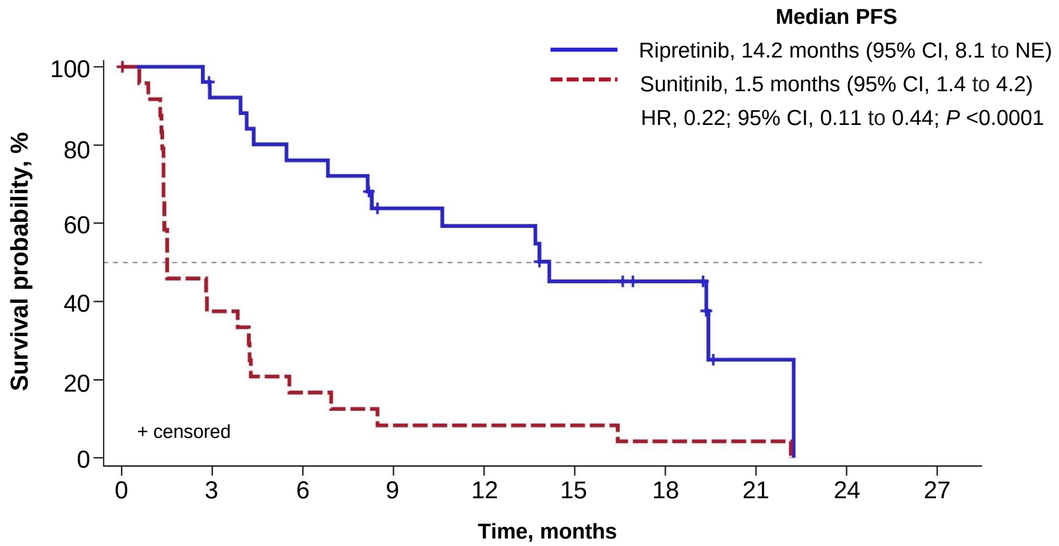
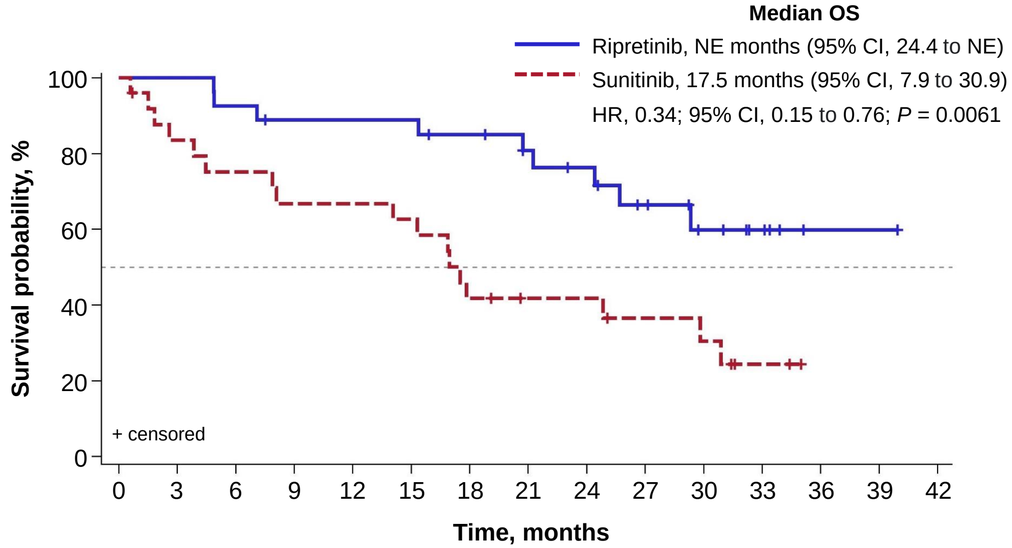
BACKGROUND

- An exploratory analysis from INTRIGUE using baseline ctDNA demonstrated meaningful clinical benefit with ripretinib vs sunitinib in patients with co-occurring *KIT* exon 11 + 17/18 mutations



Number at risk									
Ripretinib	27	23	19	14	13	9	7	1	0
Sunitinib	25	9	4	2	2	2	1	1	0



Number at risk															
Ripretinib	27	27	25	23	23	23	21	18	16	12	8	5	1	1	0
Sunitinib	25	20	18	16	16	15	10	8	8	6	5	2	0		

Bauer S, et al. *J Clin Oncol*. 2023;41(36_suppl):397784.
PFS data cutoff: September 1, 2021; OS data cutoff: September 1, 2022. Excludes *KIT* exons 9/13/14. *P*-values are nominal.
CI, confidence interval; ctDNA, circulating tumor DNA; HR, hazard ratio; NE, not estimable; OS, overall survival; PFS, progression-free survival.

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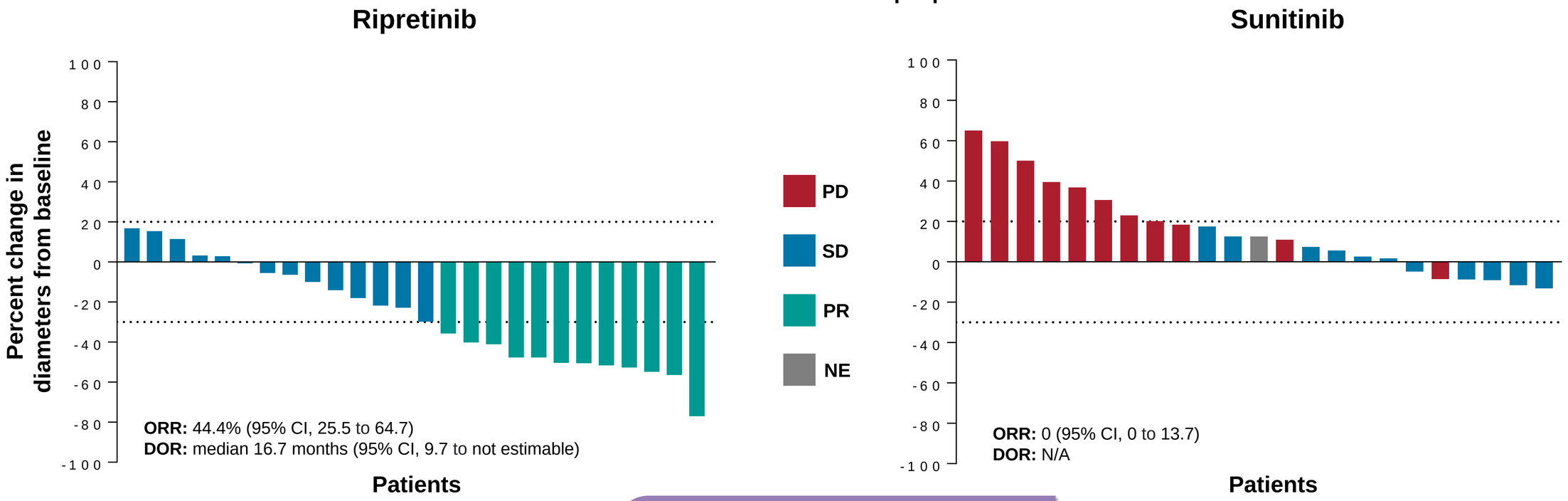
BACKGROUND

KIT exon 11 + 17/18 population



OBJECTIVE RESPONSE RATE

RIPRETINIB		SUNITINIB
44.4%	vs	**0%**

Response difference = 44.4%
95% CI, 23.0 to 62.7; nominal *P* = 0.0001

Bauer S, et al. *J Clin Oncol*. 2023;41(36_suppl):397784.
Data cutoff: September 1, 2021.
CI, confidence interval; DOR, duration of response; N/A, not applicable; NE, not evaluable; ORR, objective response rate; PD, progressive disease; PR, partial response; SD, stable disease.

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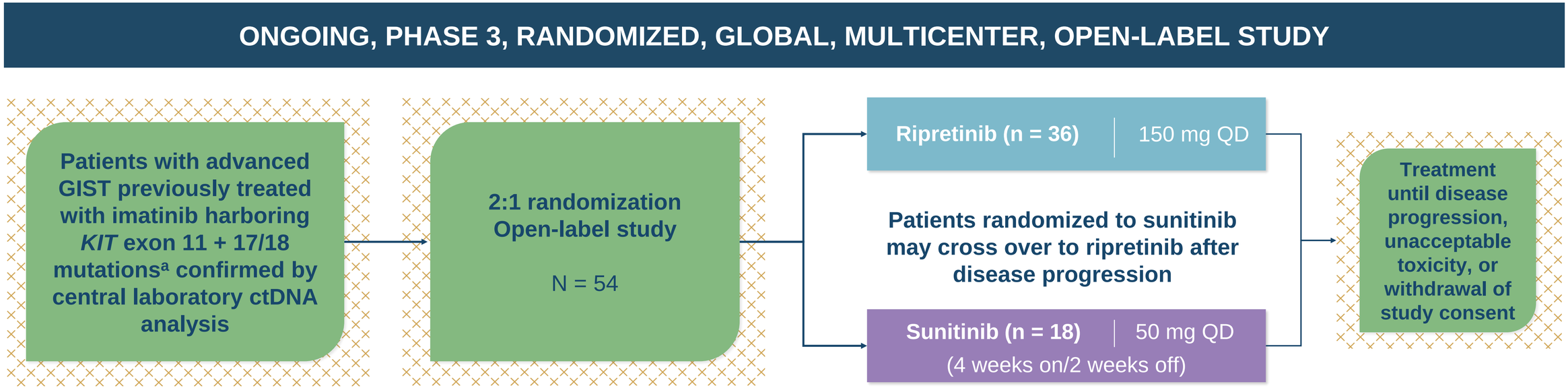
INSIGHT STUDY DESIGN



- In March 2023, FDA granted breakthrough designation to ripretinib for the treatment of adult patients with advanced GIST who received prior treatment with imatinib, and who harbor a *KIT* exon 11 mutation and co-occurring *KIT* exon 17 and/or 18 mutations (*KIT* exon 11 + 17/18 mutations)

[a]Excludes additional *KIT* primary and secondary mutations in exons 9, 13, or 14.
ctDNA, circulating tumor DNA; GIST, gastrointestinal stromal tumor; QD, once daily.

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OUTCOME MEASURES

Primary outcome measure

- PFS as determined by blinded IRR per mRECIST v1.1

Secondary outcome measures

- ORR as determined by blinded IRR using mRECIST v1.1
- OS

IRR, independent radiologic review; mRECIST v1.1, modified Response Evaluation Criteria in Solid Tumors version 1.1; ORR, objective response rate; OS, overall survival; PFS, progression-free survival.

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KEY ELIGIBILITY CRITERIA

Inclusion	Exclusion
Male or female ≥18 years of age	Co-occurring *KIT* exon 11 + 17 and/or 18 mutations that cannot be confirmed by central laboratory ctDNA analysis
Histologic diagnosis of GIST with co-occurring *KIT* exon 11 + 17 and/or 18 mutations by ctDNA analysis at prescreening confirmed by central laboratory	History of *KIT* exon 9 mutation or detection of *KIT* exon 9, 13, or 14 mutations by central laboratory ctDNA analysis
Advanced GIST and radiologic progression on imatinib treatment	Treatment with any other line of therapy in addition to imatinib for advanced GIST
Must have at least 1 measurable lesion per mRECIST v1.1 within 21 days prior to the first dose of study drug	Any prior or concurrent malignancy whose treatment may interfere with safety or efficacy assessments in this study
ECOG PS ≤2 at screening	Known active metastasis of the central nervous system

ctDNA, circulating tumor DNA; ECOG PS, Eastern Cooperative Oncology Group performance status; GIST, gastrointestinal stromal tumor; mRECIST v1.1, modified Response Evaluation Criteria in Solid Tumors version 1.1.

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CONCLUSIONS

- INSIGHT will evaluate ripretinib vs sunitinib in patients with advanced GIST previously treated with imatinib who harbor *KIT* exon 11 + 17/18 mutations
  - The primary objective of this trial is to compare the PFS of patients treated with ripretinib to that of patients treated with sunitinib
- This study may support the use of ctDNA analysis as a critical, non-invasive diagnostic tool to determine effective second-line therapies and may change how patients with advanced GIST are treated
- The INSIGHT study opened its first investigational sites in July 2023

ctDNA, circulating tumor DNA; GIST, gastrointestinal stromal tumor; PFS, progression-free survival.

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- Medical writing and editorial support were provided by Marita Chakhtoura, MS, PhD, of AlphaBioCom, a Red Nucleus company, and were funded by Deciphera Pharmaceuticals, LLC
- The INSIGHT trial-in-progress was previously presented at ASCO 2023 (George S, et al. Abstract TPS11582)

ASCO, American Society of Clinical Oncology.

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